BSBMT&CT recommendations for the management of adult patients and allogeneic donors during the COVID-19 (causative agent the SARS-CoV-2 virus) outbreak.

It is highly likely that the UK will enter into a period of high SARS-CoV-2 infection rates and COVID-19 prevalence from late-March and risks will remain high for several weeks thereafter.

The following recommendations are based on the guidance obtained from several sources including the EBMT, ASTCT, WMDA, Anthony Nolan and NHSBT. Individual centres should use these recommendations for general guidance only as circumstances will vary from centre to centre and institutional procedures should be followed. These recommendations have been produced in order to provide support to BMT teams in the UK. Advice may change as the COVID-19 prevalence increases in the UK.

Transplant teams are advised to carefully read the guidance from the EBMT and ASTCT.
EBMT guidance:
https://www.ebmt.org/sites/default/files/2020-03/EBMT%20COVID-19%20guidelines%20v.2%20%282020-03-10%29.pdf
ASTCT guidance:
https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d2-4e23-945c-45118b667268/UploadedImages/COVID-19_Interim_Patient_Guidelines_3_9_20_V2.pdf

BSBMT&CT Collaborative group advice:

Prophylaxis and treatment:
Transplant units will be familiar with the prevention of spread of respiratory viruses within their programs. It is vital that programs review and refresh their existing respiratory pathogen management procedures, policies and, for the current outbreak, align with local hospital and national policies and procedures. Patients at any time during their transplant pathway should be screened for possible upper respiratory tract infections (URTI) by careful history taking, particularly paying attention to respiratory symptoms, fevers, cough. SARS-CoV-2 appears to mainly cause fever, dry cough and sore throat with coryza occurring in only a minority of cases. Any patient pre, peri or post-transplant with respiratory symptoms should be isolated and screened for respiratory viral pathogens including SARS-CoV-2. Local guidelines must be followed for any patients identified as positive for SARS-CoV-2. Note that other respiratory viral pathogens are already known to be a serious risk to transplant recipients and if identified during screening appropriate measures should be taken including deferral of transplantation.

At this time there are no proven effective anti-viral agents recommended specifically for SARS-CoV-2, however anti-microbial therapy should be optimised with treatment directed according to any positive isolates. There is emerging evidence that part of the COVID-19 pathology is due to an inflammatory response to the virus that occurs 5-7 days following the appearance of symptoms. Several potential anti-inflammatory agents are under investigation and may be recommended in the future.

Pre-SCT:
As yet there are no recommendations for the screening of asymptomatic transplant recipients pre-transplantation. Ideally all patients should be screened before starting conditioning, as there is an asymptomatic period screening should be repeated at least twice, 1 week apart, but practice may vary between institutions. However it would be appropriate to screen transplant patients prior to the start of conditioning if they have a history of recent contact with symptomatic individuals (travel to high risk countries is rapidly becoming a redundant screening tool). As a preventative measure patients should be advised to avoid crowded places, public transport, use good hand hygiene measures and ideally remain in self-isolation for 14 days prior to the start of conditioning.

Any planned transplant should be reviewed and deferred if possible. It is anticipated that the peak risk from infection in the community will be in mid-April and may last up to 9 weeks and possibly longer. Whenever possible SCT should be deferred. This is in order to reduce the pool of high risk patients and in anticipation of a shortage of intensive care beds and possibly trained BMT unit staff.

Any patients testing positive for SARS-CoV-2 prior to SCT should be delayed by at least 3 months (ECDC recommendations), however this is not always possible due to the risk from the underlying disease. Therefore, in patients with high risk disease, HCT should be deferred until the patient is asymptomatic and has three repeated virus PCR negativity at least one week apart (deferral of 14 days minimum). In patients with low risk disease a three-month HCT deferral is recommended.

Autologous transplant recipients

- Emerging consensus that when possible autologous transplants should be deferred by at least 3 months, with case-by-case decisions. Advice may be available regarding which patients to defer and how to manage patients during the deferral period from the disease specific specialist groups, UK Myeloma Forum and Lymphoma Specialist Interest Group.
- Asymptomatic recipients should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hrs prior to the start of conditioning.
- Minimise the use of chemotherapy priming, use GCS-F alone.
- Autologous SCT for non-malignant indications should be deferred until the peak of COVID-19 passes.

Allogeneic transplant recipients

- Careful planning required for the preparative regimen as donor cells may need to be cryopreserved prior to starting condition (see donor section).
- Asymptomatic recipients should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hrs prior to the start of conditioning.
- Defer transplantation for any non-urgent indications. This will require allo-SCT MDT discussion on a case by case basis. Examples would be for MDS, MPD.
- Patients and relatives should receive instructions regarding isolation and preventative measures, this should be repeated and supported with written information.
- If close contact with COVID-19 individual immediately prior to transplant defer transplant for 3 weeks if possible (EBMT guidelines), test if symptomatic following local infection control guidelines.
- Patients who test +ve pre-SCT should be deferred where possible by at least 3 months until asymptomatic with viral throat swab negative x 3 tests, 1 week apart (EBMT guidelines). In patients with high risk disease HCT should be deferred until the patient is asymptomatic and has three repeated virus PCR negativity at least one week apart (deferral of 14 days minimum).

Allogeneic donors

- Advise sibling donors to avoid crowded public places, practise good hygiene and avoid large group gatherings for 28 days prior to donation (EBMT Guidelines). Screen donors if symptomatic and prior to starting conditioning. Advice may change soon to screen at the medical and again 2 days prior to donation. Consider harvesting sibling and cryopreserving stem cells prior to conditioning.
- Anthony Nolan recommend moving to shipping and cryopreserving stem cells before starting conditioning because of the risk of donor becoming ill and being unfit to donate plus growing uncertainties regarding transport. Liaise with local processing laboratories to warn them of each donation and whether to cryopreserve or not.
- Anthony Nolan will arrange SARS-CoV-2 testing of donor at the medical and repeated at harvest. Results should be available by the time product is cryopreserved. If not the processing laboratory may need to quarantine cryopreserved cells until results available.
- Donors will be excluded from donation for 3 months if proven COVID-19 or for 4 weeks if in close contact with COVID-19 case. Screening for SARS-CoV-2 will be required. If no suitable alternate donors and SCT urgent, perform risk assessment and lease with registry. In this situation the recipient should be involved in the discussion and be informed of the donor situation.
- In case of travel to high risk areas for COVID-19 (as defined by health authorities) or being a close contact with person travelling from such an area, donor shall be excluded from donation for at least 28 days.

- Identify back-up donor from different country or cord in case harvesting/transport of 1st donor problematic (Anthony Nolan will facilitate).
- There have been concerns that SARS-CoV-2 may be passed via blood products. Although viral RNA has been detected in blood samples of patients with COVID-19 there have been no reports of transmission of infection by blood products.

Peri and Post-transplant:

- Minimise the number of family members that visit patients. Educate all family members on hand hygiene, and how to avoid potential contact risk behaviour.
- Patients should be managed in strict protective isolation; risk assess the need for any investigations and procedures that remove the patient from their isolation room, there may be a greater risk from exposure to SARS-CoV-2 than from not having the investigation.
- Patients who are known to be SARS-CoV-2 +ve should be isolated in negative pressure cubicles wherever possible, failing this in a neutral pressure cubicle. When seeing such patients, healthcare professionals should wear full PPE including gowns, FFP3 masks, gloves and visors.
- At present it is unlikely to be feasible to screen ward staff in contact with patients routinely because of availability of testing and the pick-up rate in asymptomatic individuals is unknown.

After discharge:

- **This will be the time of greatest risk to transplant recipients.**
- At discharge reinforce need for self-isolation of the transplant recipient and if possible the immediate carer.
- Minimise clinic visits, consider how patients travel to the centre and try to reduce risks from public transport. Hospital transport may become limited.
- Set up telephone follow-up clinics, explore ways for patients to have blood tests away from busy areas in hospitals.

Staff:

- Healthcare professionals with cough/SOB/fever should not come to work. Current NHS policy does not permit screening of staff but this should change in the very near future.
- HCP who are coryzal without fever should avoid coming to work and self-isolate for at least 7 days. They should ideally be screened for respiratory viruses and SARS-CoV-2. These recommendations need to be discussed with your local Infection Control Team.
- Switch meetings/MDTs to telecons as much as possible and consider splitting workforce to mitigate risk of large proportion of team being affected at same time
- Avoid work related international travel/ large meetings

CAR-T therapy:

As yet no clear consensus. Patients are at increased risk peri- and post-treatment. Additional risk from interuption in the manufacturing chain. The pharmaceutical companies involved in the manufacture of CAR-T should be contacted directly.

Continue to check the most up to date guidelines from the donor registries and EBMT.

BSBMTCT Executive
16th March 2020